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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/781,758	02/20/2004	Neta Ilan	27525	3891

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EXAMINER	
HUTSON, RICHARD G	

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 08/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/781,758	ILAN ET AL.	
	Examiner	Art Unit	
	Richard G. Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *85-104* is/are pending in the application.

4a) Of the above claim(s) *91,92,99-102 and 104* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *85-90,93-98 and 103* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 85-104 are pending.

Election/Restriction

Applicant's election of group I, claims 87, 88 and 103 drawn to a method for regulating mammalian hair growth comprising increasing heparanase activity and applicants further election of product A: (heparanase) and SEQ ID NO: 10, in the paper of 6/7/2006, is acknowledged.

Applicants submit that the product selection and sequence selection are not separate inventions, but rather a selection of species and should the selected species be found to be patentable, the other non-elected species should be examined.

Applicant's traversal is not found persuasive on the basis that the previous requirement was a restriction requirement with the identification of certain claims as linking claims. The reasons for such were previously stated and remain. As previously stated upon the indication of allowability of the linking claims, the restriction requirement as to the linked inventions shall be withdrawn.

Claims 91, 92, 99-102, 104 are withdrawn as being drawn to a nonelected invention.

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the

list may not be incorporated into the specification but must be submitted in a separate paper."

Applicants filing of information disclosure statements, filed 4/25/2003 and4/2802005 are acknowledged. Those references considered have been initialed. It is noted that the information disclosure statement filed on 4/28/2005 contains 454 references, 51 of which are patent documents. The additional 453 references applicants say have been previously filed in parent applications. Regrettably these references have not been located and therefore have not been considered.

Specification

The disclosure is objected to because of the following informalities:

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the following reason(s): There are places within the specification where the a sequence is presented without referring to the corresponding SEQ ID NO, specifically the description of Figures 1, 16, 17, and 19.

Applicants statemtents that the instant application is a continuation of 10/341,582 is objected to because applciants do not have support for the claimed subject matter in the parent application. Thus the instant application is more accurately described as a continuation-in part of the parent application 10/341,582.

Appropriate correction is required.

Claim Objections

Claims 97 is objected to because of the following informalities:

Claims 97 is directed to non-elected subject matter (i.e. SEQ ID NOs: 13, 14, 42, 43 or 44)

Appropriate correction is required.

Claim Rejections - 35 USC ' 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 85-90, 93-98 and 103 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 85-90, 93-98 and 103 are directed to all possible methods of regulating mammalian hair growth, comprising modulating heparanase activity, heparanase level and/or heparanase expression in hair follicle cells or keratinocytes. The specification, however, provides no representative species of the claimed methods, encompassed by these claims, nor is there a disclosure of any particular structure to function/activity relationship in between heparanase treatment and regulation of mammalian hair growth. The specification also fails to describe additional representative species of the claimed

methods of use of heparanases and the heparanases necessary for the claimed methods by any identifying structural characteristics or properties other than the mere activity, for which no predictability of structure is apparent. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would not recognize Applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 85-90, 93-98 and 103 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a methods of regulating mammalian hair growth, comprising modulating heparanase activity, heparanase level and/or heparanase expression in hair follicle cells or keratinocytes, comprising administering heparanase to said cells, wherein said heparanase comprises the amino acid sequence of SEQ ID NOs: 10, does not reasonably provide enablement for any method of regulating mammalian hair growth, comprising modulating any heparanase activity, heparanase level and/or heparanase expression in hair follicle cells or keratinocytes comprising administering any heparanase. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 9-12, 14 and 16-22 are so broad as to encompass any method of regulating mammalian hair growth, comprising modulating any heparanase activity, heparanase level and/or heparanase expression in hair follicle cells or keratinocytes comprising administering any heparanase. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of proteins necessary to practice the claimed methods. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the proteins having heparanase catalytic activity wherein the proteins have the amino acid sequence of SEQ ID NO: 10 and methods of their use for regulating wound healing.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to

modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all methods of use of any heparanase protein encompassing all modifications and fragments of any protein having heparanase catalytic activity because the specification does **not** establish: (A) regions of the protein structure which may be modified without effecting heparanase catalytic activity; (B) the general tolerance of these proteins to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any method of regulating mammalian hair growth, comprising the use of any heparanase. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of those recombinant proteins having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 85-90, 93-98 and103 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Fuks et al. (U.S. Patent No: 5,362,641).

Fuks et al. disclose a heparanase derived from the human SK-HEP-1 cell line, useful for the stimulation of wound healing. Fuks et al. further teach the use of this purified heparanase and formulations containing the same in therapies such as for the stimulation and enhancement of wound healing. Fuks et al. specifically teach a method for the stimulation and enhancement of wound healing comprising administering to the wound a therapeutically effective amount of an isolated heparanase, so as to induce or accelerate the wound healing process. Fuks et al. specifically teach such methods for the treatment of cuts, burns and ulcers. It is recognized that Fuks et al. do not teach the use of the disclosed heparanase for the regulation of mammalian hair growth, however this is an inherent characteristic or result of the methods taught by Fuks et al. The heparanase of Fuks et al. is the same protein as that of the instant application, and

therefore the methods taught by Fuks et al. anticipate the methods of claims 85-90, 93-98 and103.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 85-90, 93-98 and 103 provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 9-11, 13-16, 20-22, 85-95 and 108-110 of copending Application No. 10/341,582. Although the conflicting claims are not identical, they are not patentably distinct from each other because although the conflicting claims are not identical, they are not patentably distinct from each other because claims 9-11, 13-16, 20-22, 85-95 and 108-110 of 10/341,582. drawn to methods comprising administering heparanase anticipates claims 85-90, 93-98 and 103 drawn to methods comprising administering heparanase.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (571) 272-0930. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (571) 272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Richard G Hutson, Ph.D.
Primary Examiner
Art Unit 1652

rgh
8/16/2006